intermolecular crosslinking reactions were to be avoided. In addition, it was also intended to be able to link active ingredients which have phosphate groups.

It was therefore also an object of the present invention to indicate compounds which permit coupling as selectively as possible to the active ingredient. Thus, it was intended in particular to be able to adjust a specific stoichiometry of the conjugate, it being specifically intended to make it possible to prepare 1:1 conjugates through the use of these compounds.

Finally, the invention was based on the object of providing a method which is as simple and cost-effective as possible for preparing such compounds and coupling products of polysaccharides or polysaccharide derivatives with active ingredients.

These objects and others which, although not mentioned verbatim, can be inferred as self-evident from the contexts discussed herein, or are automatically evident therefrom, are achieved with the aldonic acid esters described in claim 1. Expedient modifications of these aldonic acid esters according to the invention, and stable aldonic acid esters which can be employed in methods for preparing conjugates, are protected by dependent claims 2-17 which refer back to claim 1.

In relation to a method for preparing the aldonic acid esters, claims 18-27 provide an achievement of the underlying object.

Claims 28-32 describe methods for preparing polysaccharide-active ingredient conjugates and the pharmaceutical active ingredients obtainable by these methods.

The provision of aldonic acid esters which are derived from polysaccharides or polysaccharide derivatives which are selectively oxidized at the reducing end of the chain to aldonic acids allows compounds which achieve the aforementioned objects to be provided. Such esters can be regarded as activated acids. They react in an aqueous medium with nucleophilic NH2 groups to give (more stable) amides.

Claims

1. An aldonic acid ester of polysaccharides or polysaccharide derivatives which are selectively oxidized at the reducing end of the chain to aldonic acids.

2. The aldonic acid ester as claimed in claim 1, characterized in that the polysaccharides or polysaccharide derivatives are starch fractions or starch fraction derivatives.

3. The aldonic acid ester as claimed in claim 2, characterized in that the starch fractions are amylopectin degradation fractions.

4. The aldonic acid ester as claimed in claim 3, characterized in that the amylopectin degradation fractions are obtained by acid degradation and/or degradation by a-amylase of waxy corn starch.

5. The aldonic acid ester as claimed in claim 4, characterized in that the starch fractions have an average molecular weight Mw of 2000-50 000 Dalton and an average branching of 5-10 mol% a-1,6-glycosidic linkages.

6. The aldonic acid ester as claimed in claim 4, characterized in that the starch fractions have an average molecular weight Mw of 2000-50 000 Dalton and an average branching in the range from > 10 to 25 mol% a-1,6-glycosidic linkages.

7. The aldonic acid ester as claimed in claim 2, characterized in that the starch fraction derivatives are hydroxyethyl derivatives of waxy corn starch degradation fractions.

8. The aldonic acid ester as claimed in claim 7, characterized in that the average molecular weight Mw of the hydroxyethyl starch fractions is in the range of 2-300 000 Dalton, and the substitution level MS is between 0.1 and 0.8, and the C2/C6

ratio of the substituents on carbon atoms C2 and C6 of the anhydroglucoses is between 2 and 15.

9. The aldonic acid ester as claimed in at least one of claims 1 to 8, characterized in that the alcohol from which the alcohol component of the aldonic acid ester is derived has a molecular weight in the range from 80 to 500 g/mol.

10. The aldonic acid ester as claimed in at least one of claims 1 to 9, characterized in that the alcohol from which the alcohol component of the aldonic acid ester is derived has a pka in the range from 6 to 12.

11. The aldonic acid ester as claimed in at least one of claims 1 to 10, characterized in that the alcohol from which the alcohol component of the aldonic acid ester is derived, of the aldonic acid ester, includes an HO-N group or a phenol group.

12. The aldonic acid ester as claimed in at least one of claims 1 to 11, characterized in that the alcohol from which the alcohol component of the aldonic acid ester is derived is selected from N-hydroxysuccinimide, sulfo-N-hydroxysuccinimide, substituted phenols and hydroxybenzotriazole.

13. The aldonic acid ester as claimed in claim 12, characterized in that the alcohol from which the alcohol component of the aldonic acid ester is derived is N-hydroxysuccinimide and sulfo-N-hydroxysuccinimide.

14. A solid comprising at least one aldonic acid ester as claimed in at least one of claims 1 to 13.

15. A solution comprising at least one aldonic acid ester as claimed in at least one of claims 1 to 13.

16. The solution as claimed in claim 15, characterized in that the solution comprises at least one organic solvent.

17. The solution as claimed in claim 16, characterized in that the solution comprises not more than 0.5% by weight water.

18. The solution as claimed in at least one of claims 15 to 17, characterized in that the solution comprises at least one aprotic solvent.

19. The solution as claimed in claim 18, characterized in that the solvent comprises dimethyl sulfoxide (DMSO), N-methylpyrrolidone, dimethylacetamide (DMA) and/or dimethylformamide (DMF).

20. A method for preparing aldonic acid ester as claimed in at least one of claims 1 to 19, characterized in that at least one aldonic acid and/or one aldonic acid derivative is reacted with at least one alcohol component in aprotic solvent.

21. The method as claimed in claim 20, characterized in that the alcohol component is employed in 5 to 50-fold molar excess based on the aldonic acid and/or the aldonic acid derivative.

22. The method as claimed in claim 20 or 21, characterized in that the reaction takes place with the use of at least one activating reagent.

23. The method as claimed in claim 22, characterized in that the activating reagent comprises at least one carbodiimide.

24. The method as claimed in at least one of claims 22 or 23, characterized in that the activating reagent is employed in 1- to 3-molar excess based on the aldonic acid and/or the aldonic acid derivative.

25. The method as claimed in at least one of claims 20 to 24, characterized in that a compound which liberates an alcohol component for reaction with the aldonic acid or the aldonic acid derivative is employed.

26. The method as claimed in claim 25, characterized in that a carbonic diester is employed.

27. The method as claimed in at least one of claims 20 to 26, characterized in that the reaction takes place at a temperature in the range from 0 to 40°C.

28. The method as claimed in at least one of claims 20 to 27, characterized in that the reaction takes place at a low base activity.

29. A method for preparing pharmaceutical active ingredients coupled to polysaccharides or polysaccharide derivatives on free amino functions, characterized in that at least one aldonic acid ester as claimed in any of claims 1 to 13 is reacted with a pharmaceutical active ingredient which has at least one amino group.

30. The method as claimed in claim 29, characterized in that the reaction takes place in aqueous medium.

31. The method as claimed in claim 30, characterized in that the pH of the aqueous medium is in the range from 7 to 9.

32. The method as claimed in at least one of claims 29 to 31, characterized in that the reaction takes place at a temperature in the range from 0°C to 40°C.

33. The method as claimed in at least one of claims 29 to 32, characterized in that the pharmaceutical active ingredient is a polypeptide or a protein.

34. A pharmaceutical active ingredient obtainable by a method as claimed in at least one of claims 29 to 33.